

**IN THE CLAIMS:**

Please cancel claims 71, 73 and, 133-135, 140-143, 146, and 149; amend claims 64 and 65; and add new claims 166-174.

This listing of claims will replace all prior versions, and listings of the claims in the application.

**Listing of the claims**

1-63. **(Canceled)**

64. **(Currently Amended)** A method of inducing a cytostatic effect in a primary or metastasized colorectal, gastric or esophageal cancer cell in an individual who has been identified as having primary or metastasized colorectal, gastric or esophageal cancer, said method comprising the step of: administering ~~to said individual by infusion into the circulatory system~~ of said individual, a cytostatically effective amount of [[a]] an unconjugated guanylyl cyclase C ligand sufficient to have a therapeutic effect, wherein the cytostatically effective amount of an unconjugated guanylyl cyclase C ligand is an amount sufficient to maintain a concentration  $\geq EC_{50}$  of said unconjugated guanylyl cyclase C ligand for at least 15 days, by the ~~cytotoxic effect of the guanylyl cyclase C~~, wherein [[a]] an unconjugated guanylyl cyclase C ligand molecules bind to guanylyl cyclase C on the surface of a primary or metastasized colorectal, gastric or esophageal cancer cell in said individual and induce a cystostatic effect in said cells.

65. **(Currently Amended)** A method of inhibiting the proliferation of a primary or metastasized colorectal, gastric or esophageal cancer cell in an individual who has been identified as having primary or metastasized colorectal, gastric or esophageal cancer, said method comprising the step of: administering ~~to~~ into the circulatory system of said individual, ~~by~~

~~infusion~~, a cytostatically effective amount of ~~[[a]]~~ an unconjugated guanylyl cyclase C ligand sufficient to have a therapeutic effect, wherein the cytostatically effective amount of an unconjugated guanylyl cyclase C ligand is an amount sufficient to maintain a concentration  $\geq EC_{50}$  of said unconjugated guanylyl cyclase C ligand for at least 15 days, ~~by the cytostatic effect of the guanylyl cyclase C ligand,~~ wherein said unconjugated guanylyl cyclase C ligand molecules bind to guanylyl cyclase C on the surface of a primary or metastasized colorectal, gastric or esophageal cancer cell in said individual and inhibit ~~induce~~ proliferation of said cells.

66-67. **(Canceled)**

68. **(Previously presented)** The method of claim 64 or 65 further comprising the step of administering a different therapeutic agent.

69. **(Previously presented)** The method of claim 68 wherein the therapeutic agent is 5-fluorouracil.

70. **(Previously presented)** The method of claim 68 wherein the therapeutic agent is bleomycin.

71. **(Canceled)**

72. **(Previously presented)** The method of claim 64 or 65 wherein said guanylyl cyclase C ligand is administered intravenously.

73. **(Canceled)**

74. **(Previously presented)** The method of claim 64 or 65 wherein said guanylyl cyclase C ligand is an anti-guanylyl cyclase C antibody or an anti-guanylyl cyclase C binding fragment thereof.

75. **(Previously presented)** The method of claim 74 wherein said guanylyl cyclase C ligand is an anti-guanylyl cyclase C monoclonal antibody.

76-90. **(Canceled)**

91. **(Previously presented)** The method of claim 64 or 65 wherein said guanylyl cyclase C ligand is initially administered to said individual in a loading dose of at least 0.1nM per 10 kg. bodyweight of said individual.

92. **(Previously presented)** The method of claim 64 or 65 wherein said loading dose is 0.1 -10nM of guanylyl cyclase C ligand per 10 kg. bodyweight of said individual.

93. **(Previously presented)** The method of claim 64 or 65 wherein said loading dose is 0.5-8nM of guanylyl cyclase C ligand per 10 kg. bodyweight of said individual.

94. **(Previously presented)** The method of claim 64 or 65 wherein said loading dose is 1-5nM of guanylyl cyclase C ligand per 10 kg. bodyweight of said individual.

95. **(Previously presented)** The method of claim 64 or 65 wherein said guanylyl cyclase C ligand is infused into said individual in a dose of .1 -10nM of ST receptor ligand per 10 kg. bodyweight of said individual.

96. **(Previously presented)** The method of claim 64 or 65 wherein said guanylyl cyclase C ligand is infused into said individual in a dose of .5-8nM of guanylyl cyclase C ligand per 10 kg. bodyweight of said individual.

97. **(Previously presented)** The method of claim 64 or 65 wherein said guanylyl cyclase C ligand is infused into 30 said individual in a dose of 1.5nM of guanylyl cyclase C ligand per 10 kg. bodyweight of said individual.

98. **(Previously presented)** The method of claim 64 or 65 wherein said guanylyl cyclase C ligand is infused into said individual for at least 8 hours.

99. **(Previously presented)** The method of claim 64 or 65 wherein said guanylyl cyclase C ligand is infused into said individual for at least 12 hours.

100. **(Previously presented)** The method of claim 64 or 65 wherein said guanylyl cyclase C ligand is infused into said individual for at least 16 hours.

101. **(Previously presented)** The method of claim 64 or 65 wherein said guanylyl cyclase C ligand is infused into said individual for at least 20 hours.

102. **(Previously presented)** The method of claim 64 or 65 wherein said guanylyl cyclase C ligand is infused into said individual for at least 24 hours.

103. **(Previously presented)** The method of claim 64 or 65 further comprising administering calcium to said individual.

104-131. **(Canceled)**

132. **(Previously presented)** The method of claim 64 wherein at least 0.1-10nM of an guanylyl cyclase C ligand per 10 kg. bodyweight of said individual are administered per hour for at least 6 hours, and a therapeutic pharmaceutical composition that comprises components which target guanylyl cyclase C for delivery of a therapeutic agent is further administered to said individual.

133 - 144. **(Canceled)**

145. **(Previously presented)** The method of claim 75 wherein said guanylyl cyclase C ligand is a humanized anti-guanylyl cyclase C monoclonal antibody.

146. **(Canceled)**

147. **(Previously presented)** The method of claim 103 further comprising the step of administering a different therapeutic agent.

148. **(Previously presented)** The method of claim 103 wherein the therapeutic agent is 5-fluorouracil.

149. **(Cancelled)**

150. **(Previously presented)** The method of claim 103 wherein said guanylyl cyclase C ligand is administered intravenously.

151. **(Previously presented)** The method of claim 103 wherein said guanylyl cyclase C ligand is an anti-guanylyl cyclase C antibody or an anti-guanylyl cyclase C binding fragment thereof.

152. **(Previously presented)** The method of claim 103 wherein said guanylyl cyclase C ligand is an anti-guanylyl cyclase C monoclonal antibody.
153. **(Previously presented)** The method of claim 103 wherein said guanylyl cyclase C ligand is initially administered to said individual in a loading dose of at least 0.1nM per 10 kg. bodyweight of said individual.
154. **(Previously presented)** The method of claim 103 wherein said loading dose is 0.1 -10nM of guanylyl cyclase C ligand per 10 kg. bodyweight of said individual.
155. **(Previously presented)** The method of claim 103 wherein said loading dose is 0.5-8nM of guanylyl cyclase C ligand per 10 kg. bodyweight of said individual.
156. **(Previously presented)** The method of claim 103 wherein said loading dose is 1-5nM of guanylyl cyclase C ligand per 10 kg. bodyweight of said individual.
157. **(Previously presented)** The method of claim 103 wherein said guanylyl cyclase C ligand is infused into said individual in a dose of .1 -10nM of ST receptor ligand per 10 kg. bodyweight of said individual.
158. **(Previously presented)** The method of claim 103 wherein said guanylyl cyclase C ligand is infused into said individual in a dose of .5-8nM of guanylyl cyclase C ligand per 10 kg. bodyweight of said individual.
159. **(Previously presented)** The method of claim 103 wherein said guanylyl cyclase C ligand is infused into 30 said individual in a dose of 1.5nM of guanylyl cyclase C ligand per 10 kg. bodyweight of said individual.

160. **(Previously presented)** The method of claim 103 wherein said guanylyl cyclase C ligand is infused into said individual for at least 8 hours.

161. **(Previously presented)** The method of claim 103 wherein said guanylyl cyclase C ligand is infused into said individual for at least 12 hours.

162. **(Previously presented)** The method of claim 103 wherein said guanylyl cyclase C ligand is infused into said individual for at least 16 hours.

163. **(Previously presented)** The method of claim 103 wherein said guanylyl cyclase C ligand is infused into said individual for at least 20 hours.

164. **(Previously presented)** The method of claim 103 wherein said guanylyl cyclase C ligand is infused into said individual for at least 24 hours.

165. **(Previously presented)** The method of claim 152 wherein said guanylyl cyclase C ligand is a humanized anti-guanylyl cyclase C monoclonal antibody.

166. **(New)** The method of claim 64 or 65 wherein said guanylyl cyclase C ligand is infused into said individual for at least 6 hours.

167. **(New)** The method of claim 64 or 65 wherein the amount of a guanylyl cyclase C ligand administered is an amount sufficient to maintain a concentration  $\geq EC_{50}$  of said guanylyl cyclase C ligand for at least 30 days.

168. **(New)** The method of claim 64 or 65 wherein the individual has been identified as having metastatic colorectal, esophageal or stomach cancer.

169. **(New)** A method of killing primary or metastasized colorectal, gastric or esophageal cancer cells in an individual who has been identified as having primary or metastasized colorectal, gastric or esophageal cancer, said method comprising the steps in the following order:

a) administering to said individual a cytostatically effective amount of a guanylyl cyclase C ligand sufficient to inhibit cell proliferation h by the cytostatic effect of the guanylyl cyclase C ligand, wherein guanylyl cyclase C ligand molecules bind to guanylyl cyclase C on the surface of a primary or metastasized colorectal, gastric or esophageal cancer cell in said individual and inhibit proliferation of said cells and wherein the cytostatically effective amount of a guanylyl cyclase C ligand is an amount sufficient to maintain a plasma concentration  $\geq EC_{50}$  of said guanylyl cyclase C ligand and

b) subsequently administering a different therapeutic agent.

170. **(New)** A method of killing primary or metastasized colorectal, gastric or esophageal cancer cells in an individual who has been identified as having primary or metastasized colorectal, gastric or esophageal cancer, said method comprising the steps in the following order:

a) administering to said individual an anti-guanylyl cyclase C antibody or a guanylyl cyclase C binding fragment thereof; and

b) subsequently administering a different therapeutic agent.

171. **(New)** The method of claim 169 or 170, wherein said different therapeutic agent is selected from the group consisting of: methotrexate, doxorubicin, daunorubicin, cytosinarabioside, etoposide, 5- fluorouracil, melphalan, chlorambucil, cis-platin, vindesine, mitomycin, bleomycin, purothionin, macromomycin, 1,4 benzoquinone derivatives, trenimon,



ricin, ricin A chain, Pseudomonas exotoxin, diphtheria toxin, Clostridium perfringens phospholipase C, bovine pancreatic ribonuclease, pokeweed antiviral protein, abrin, abrin A chain, cobra venom factor, gelonin, saporin, modeccin, viscumin, volkensin, nitroimidazole, metronidazole and misonidazole.

172. **(New)** The method of claim 169 or 170, wherein the individual has been identified as having metastatic colorectal, esophageal or stomach cancer.

173. **(New)** The method of claim 170 wherein said an anti-guanylyl cyclase C antibody is a humanized anti-guanylyl cyclase C monoclonal antibody.

174. **(New)** The method of claims 64, 65, or 171, wherein the cytostatically effective amount of a guanylyl cyclase C ligand is an amount sufficient to maintain a concentration of greater than or equal to 10 times the  $EC_{50}$  of said guanylyl cyclase C ligand.